AMENDMENTS TO THE DRAWINGS

Please replace Fig. 21 with the attached amended drawing, in which SEQ ID Nos. have been added.

Attachment: Replacement Sheet

REMARKS

Sequence Compliance

The Examiner alleged that Figures 20 and 21 contain sequences not identified by sequence identifier numbers. Applicants herein submit a substitute Fig. 21 and an amendment to the Brief Description of Fig. 20, which include SEQ ID Nos. Applicants also herein submit a substitute paper copy of the sequence listing, an amendment directing its entry into the specification, a CRF, and letter stating that the contents of the sequence listing and the CRF are the same and contain no new matter. Applicants therefore request withdrawal of the objection.

Remarks to the Drawings

Fig. 21 has been amended to add SEQ ID Nos. Applicants assert that no new matter has been introduced.

Remarks to the Specification

The amendments to the specification add in SEQ ID Nos. and are editorial in nature. Applicants assert that no new matter has been introduced.

Information Disclosure Statement

The Examiner alleged that articles crossed out by the Examiner on the Information Disclosure Statement filed May 31, 2006 were not considered by the Examiner, because the references were not located. Applicants maintain that the references in question were submitted with the Information Disclosure Statement filed November 16, 2004, and were initialed by the Examiner on the November 16, 2004 form. Accordingly, the Examiner has already considered those references.

Remarks to the Declaration

The Examiner objected to the Declaration because there were allegedly un-initialed changes in Himangi Jayakar's address. Applicants attach hereto a supplemental Declaration. Accordingly, Applicants request withdrawal of the objection.

Status of Claims

Claims 1-112 are pending in the application, of which claims 9-14, 19-29, 38-41, 46, 48, 51-56, 63-74, 76, 78, 86-88, and 92-112 have been withdrawn from consideration due to a restriction requirement by the Examiner. Applicants note that claim 63 has been corrected to depend on a non-withdrawn claim, and therefore request that it be rejoined. The Examiner objected to claims 5, 34, 45, and 75. Claims 1-8, 15-18, 30-37, 42-45, 47, 49, 50, 57-62, 75, 77, 79-85, and 89-91 have been rejected. Claims 1, 2, 4-10, 16, 18-22, 26, 27, 30, 31, 33-38, 42, 43, 45, 47, 49-51, 57-59, 62-64, 71, 72, 75-77, 79, 80, 82, 84, 85, 89, 90, 92, 94, 96, 98, 100, and 102 have been amended. Amendments to claims 1, 2, 4-10, 16, 18-22, 26, 27, 30, 31, 33-38, 42, 43, 45, 47, 49-51, 57-59, 62-64, 71, 72, 75-77, 79, 80, 82, 84, 85, 89, 90, 92, 94, 96, 98, 100, and 102 are clerical in nature. Support for amendments to claims 4 and 16 can be found throughout the specification as originally filed and specifically in claim 26 as originally filed and on page 12, paragraphs 129-130. Applicants assert that no new matter has been introduced.

Claims 17 and 61 have been cancelled without prejudice or disclaimer. Applicants reserve all rights in these claims to file divisional and/or continuation patent applications.

Claim Objections

In the Office Action, the Examiner objected to claims 5, 34, 45, and 75 because of alleged informalities. Claims 5, 34, 45, and 75 were amended as required by the Examiner to cure these informalities. Accordingly, Applicants request withdrawal of the objection.

CLAIM REJECTIONS

35 U.S.C. § 112 Rejections

In the Office Action, the Examiner rejected claims 6-8, 16, 17, 35-37, 42, 47, 49, 50, 58, 59, 61, 62, 77, 79-82, 84, 85, and 89 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner alleged that the metes and bounds of the mutations and deletions in claims 6, 35, 47, 77, and 82 are unclear. Applicants disagree. Claims 6, 35, and 82 are dependent on claims 1, 30, and 81, respectively, which identify that the deletion or mutation

is within the Rhabdoviral matrix protein. Claims 47 and 77 are dependent on claims 45 and 75, respectively, which identify that the deletion or mutation is within the membrane-proximal ectodomain of the Rhabdoviral glycoprotein. However, to expedite prosecution, Applicants have amended the claims to reiterate the protein in which the listed mutations occur. Applicants therefore request withdrawal of the rejection.

Claims 7, 36, 49, and 84 were rejected as allegedly referring to a "second polypeptide" for which there was no antecedent basis for a first polypeptide. Claims 7, 36, 49, and 84 do not refer to a second polypeptide. Applicants therefore request withdrawal of the rejection.

Claims 16, 61, and 62 were rejected as allegedly referring to a use without providing any steps involved in the method or process. Claim 61 was cancelled, rendering the rejection moot. Claims 16 and 62 do not refer to a use. Applicants therefore request withdrawal of the rejection.

Claim 17 was rejected as allegedly being indefinite. Claim 17 has been cancelled, rendering the rejection moot.

The Examiner rejected claims 31 and 42 and alleged that the relationship of the isolated nucleic acid and protein is unclear. In claims 31 and 42, the nucleic acid molecule comprises a polynucleotide or nucleic acid sequence encoding a protein or polypeptide. Applicants therefore request withdrawal of the rejection.

Claim 58 was rejected as allegedly failing to have sufficient antecedent basis for the expression "said genetically modified matrix protein." Claim 58 does not comprise the cited expression. Applicants therefore request withdrawal of the rejection.

Claim 59 was rejected as allegedly having incorrect dependency. Claim 59 correctly depends on claim 58, and the limitations of the claim have sufficient antecedent basis therein. Applicants therefore request withdrawal of the rejection.

Claim 75 was rejected as allegedly being unclear in its recitation of "a gene encoding a membrane-proximal ectodomain". Claim 75 refers to "a polynucleotide encoding the membrane-proximal ectodomain." Applicants therefore request withdrawal of the rejection.

Claim 79 was rejected as allegedly being vague in that it was unclear if the recited non-cytopathic genome is the same Rhabdovirus genome as recited in claim 75 or a second genome. Claim 79 specifies that the Rhabdovirus genome as recited in claim 75 further comprises a deletion or mutation with the M protein, wherein said mutation or deletion results in a non-cytopathic Rhabdovirus. Applicants therefore request withdrawal of the rejection.

Claims 80-82 were rejected as allegedly not limiting the mutations recited in claim 75. However, claims 80-82 limit the mutations recited in claim 79. Applicants therefore request withdrawal of the rejection.

Claim 80 was rejected as allegedly having insufficient antecedent basis for "said matrix protein." Applicants disagree. Claim 80 is dependent on claim 79, which recites "a matrix protein." Applicants therefore request withdrawal of the rejection.

The Examiner alleged that the relationship of the isolated nucleic acid and protein is unclear in claim 89. However, the nucleic acid molecule in claim 89 comprises a nucleic acid sequence encoding a protein or polypeptide. Applicants therefore request withdrawal of the rejection.

In the Office Action, the Examiner rejected claims 6, 35, 47, 77, and 82 under 35 U.S.C. § 112, first paragraph, as allegedly not meeting the enablement requirement.

Applicants wish to thank the Examiner for admitting that the specification is enabling for recombinant VSV M protein with an alanine to methionine substitution at position 33 or 51 or a serine for glycine substitution at position 226 of the protein and for a deletion of amino acids 440-449 in VSV glycoprotein. The Examiner alleged that both matrix and G proteins vary between Rhabdovirus species, especially between Rhabdovirus species found in mammals versus those found in plants and insects. Applicants disagree. A person of skill in the art at the time of the invention would be able to identify important corresponding residues across species, even if there was a low sequence homology between species (see, for example, Figure 20). A person of skill in the art at the time of the invention would be able to identify matrix proteins of various Rhabdoviruses via their size, function, and/or antibody reactivity, align them using technology and knowledge available at the time by use of

common motifs, domains, and conserved residues, and understand which nucleotides to modify within the matrix protein based on the enabling disclosure of the instant application (for example, see Taylor et al, 1999 cited by the Examiner in the November 14, 2006 office action). Further, the particular residues shown to be important for cytopathic effects of the matrix proteins were found to be conserved across Rhabdovirus species (Taylor et al page 224, right column, 2nd paragraph).

Thus, in light of the specification and level of skill in the art at the time of filing, Applicants assert that the claims are enabled for mutations in any Rhabdovirus species and therefore request withdrawal of the rejection.

35 U.S.C. § 102 Rejections

The Examiner rejected claims 1-5, 7, 8, 15-18, 30-34, 36, 37, 43-45, 47, 49, 50, 57, 58, 60-62, 75, 77, 79-81, 83-85, and 89-91 of the instant application under 35 USC 102(e) as allegedly being anticipated by Bell *et al.* (2004/0170607). The M protein mutations of the instant invention, which result in a non-cytopathic Rhabdovirus are inherently different than the multiple mutations of Bell *et al.*, in which mutants are selected which grow poorly on interferon-responsive cells. The nature of the mutations differs, because the criteria for mutant selection differ, and therefore the claims are not anticipated by Bell.

Other claims of the instant invention are drawn to a G protein with a deletion or mutation of the membrane-proximal ectodomain of the G protein, which results in a Rhabdovirus with decreased viral membrane fusion. In contrast, Bell describes random mutations throughout the VSV genome, including, but not solely, in the G protein, for identifying VSV mutants that grow poorly on interferon-responsive cells. Bell does not mention nor acknowledge the importance of the membrane-proximal ectodomain of the G protein for inhibiting Rhabodovirus growth on interferon-responsive cells, and **certainly not** for inhibiting viral membrane fusion. It was therefore unexpected in light of Bell that mutations of the membrane-proximal ectodomain of the G protein inhibit membrane fusion. Therefore, Bell does not anticipate nor render obvious the instant claims. Applicants therefore request withdrawal of the rejection.

The Examiner rejected claims 1-3, 7, 8, 15, 16, 18, 30, 32, 36, 37, 43-45, 47, 49, 50, 60-62, 75, 77, 83-85, and 89-91 of the instant application under 35 USC 102(b) as allegedly being anticipated by Conzelmann (US 6,033,886). Applicants disagree. Conzelmann selected M protein mutants that reduced host cell attachment and membrane fusion (column 5, line 40) to create a non-infectious rabies vaccine (column 6, line 10), whereas the selection criteria in the instant invention were Rhabdoviruses with a mutant M protein demonstrating infection without cytopathic effects. Therefore, the mutants of Conzelmann and those of the instant invention are inherently different, based on distinct selection criteria. Further, based on Conzelmann, one of skill in the art would not find credible that M protein mutants can form infectious viruses (column 6, line 10), which was demonstrated in the instant invention.

Other claims of the instant invention are drawn to a Rhabdovirus with a deletion or mutation of the membrane-proximal ectodomain of the G protein, which results in a Rhabdovirus with decreased viral membrane fusion. In contrast, Conzelmann describes mutations in the G protein or deletions of the entire G protein, for producing non-infectious rabies virus. Conzelmann neither mentions nor acknowledges the importance of any specific portion of the G protein, and certainly not the membrane-proximal ectodomain of the G protein, for inhibiting infection in G protein mutant rabies viruses. Therefore, Conzelmann does not anticipate the instant claims. Applicants therefore request withdrawal of the rejection.

Provisional Obviousness-Type Double Patenting Rejections

The Examiner provisionally rejected claims 45, 75, and 90 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 7, 8, and 28 of copending Application No. 10/274,359. Applicants note that the 10/274,359 (our reference: P-3182-US3) patent application has been abandoned, rendering the rejection moot.

The Examiner provisionally rejected claims 45, 47, 49, 61, 75, 77, 83, 84, and 89-91 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 10/327,673. Applicants note that because the rejection is provisional, Applicants need not address the rejection until the claims of the pending '673 Application are allowed. In addition, the 10/327,673 Application claims a recombinant Rhabdovirus comprising a deletion of the N-terminal portion of the G protein sequence (for example, amino acids 1-404) and an insertion of the G stem polypeptide

(comprising, *inter alia*, the carboxy terminus of the membrane proximal ectodomain of the G protein). Thus, only a C-terminal fragment of the G protein is within the scope of the claims of the 10/327,673 Application. In contrast, the subject Application claims constructs comprising the N-terminal sequence of G protein with a deletion in the membrane-proximal ectodomain. There is no overlap between the G segments contained in the 10/327,673 and subject Applications. Accordingly, such a rejection is inappropriate.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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Dated: 15 March , 2007

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